REMARKS

In response to the Office Action mailed December 18, 2003 (hereafter referred to as "Office Action"), Applicant respectfully requests re-examination of the claims and reconsideration of the Examiner's rejection of the claims of the above-identified application.

Claims 1-26 are pending in the Application.

Claims 1, 3, 18, and 26 have been amended.

Claims 2, 9, and 19 have been cancelled.

INTERVIEW WITH EXAMINER

Pursuant to Applicant's April 9, 2004 interview with Examiner Choi, Applicant has amended all independent claims to require at least about 5.0% (w/v) pre-treated ascorbic acid, having a pH of 3.5 to 4.1, and not having any chemical stabilizers. Furthermore, Applicant attaches hereto, as Exhibit A, the requested Affidavit detailing the actual content of ascorbic acid in the final admixed compositions of Duffy et al., U.S. Patent 5,516,793.

CLAIM REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 1-3, 10, 15-18, 24, and 25 have been rejected under 35 U.S.C. § 102(b) as being unpatentable over Duffy et al. ("*Duffy*") (U.S. Patent 5,516,793). Applicant respectfully traverses the 35 U.S.C. § 102(b) rejections as such rejections pertain to the cited claims.

The Examiner has stated that *Duffy* expressly discloses a composition comprising demineralized water, propylene glycol, glycerin, hydroxyethylcellulose, Tween 20, ammonium hydroxide, glycolic acid and ascorbic acid (5% or 10%), having a pH of 3.7 (5%) and 3.8 (10%). The Examiner has also stated that with respect to claim 24, the term "about 15%" is not defined, as such, the Examiner has read the term "about" to include 10%. *See* Office Action, page 2, fourth full paragraph.

As stated above, independent claims 1 and 18 have been amended to require at least about 5.0% (w/v) pre-treated ascorbic acid, having a pH of 3.5 to 4.1, and not having any chemical stabilizers.

Claim 2 has been cancelled.

Claim 3 has been amended to maintain proper claim dependency.

As amended, all of the above-rejected, still pending claims require a composition comprising at least 5.0% (w/v) pre-treated ascorbic acid in water, and a pH of 3.5 to 4.1. Such compositions, comprising relatively high pH values for such relatively high concentrations of ascorbic acid, are made possible by the stabilizing pre-treatments described in Application. Without such treatments, the ascorbic acid rapidly degrades at pH values greater than 3.5 to yield solutions that comprise less than 5.0%(w/v) ascorbic acid. With regard to *Duffy*, Applicant respectfully points out that the Examiner is assuming that there is no reaction of components within the mixtures and that the resulting compositions of *Duffy* are simply the sum of the initial components. Reaction of the components of *Duffy* does occur, however, and the resulting compositions disclosed therein do not comprise at least 5.0% (w/v) ascorbic acid in the admixed formulation.

Duffy describes the addition of ascorbic acid to topical formulations for the purpose of reducing irritation caused by another active ingredient. Unlike in the compositions of the present invention, however, ascorbic acid is not the active ingredient in the compositions of *Duffy*. Referring to *Duffy*, col. 7, ll. 8-31 (Example II), Compositions E and F are formulated (in part) with 5 and 10wt.% ascorbic acid, and have resulting pH values of 3.7 and 3.8, respectfully. However, in each of these compositions, sufficient base (ammonium hydroxide) is added to convert all or most of the ascorbic acid present in the formulation to the unstable ascorbate anion (with is easily oxidized). For example, in Composition E, there is roughly three times as much NH_4OH (on a mole basis) as ascorbic acid. Even if it is assumed that the NH_4OH preferentially "neutralizes" all of the glycolic acid present, there is still enough NH_4OH present to convert more than 85% of the ascorbic acid to the ascorbate anion. For Composition F, there is enough NH_4OH present to convert all of both the glycolic acid and ascorbic acid to their conjugate base forms (the ascorbate anion in the case of ascorbic acid). Thus, such compositions of *Duffy* cannot be expected to comprise any more than about 1wt.% ascorbic acid in their final admixed form.

As a result of the foregoing, Applicant respectfully requests that the Examiner withdraw the rejection of Claims 1,3, 10, 15-18, 24, and 25 under 35 U.S.C. § 102(b) as being unpatentable over Duffy et al.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 1-26 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Schinitsky et al. ("*Schinitsky*") (U.S. Patent 4,938,969) in view of Murad ("*Murad*") (U.S. Patent 5,804,594), Herstein ("*Herstein*") (U.S. Patent 5,902,591) and Taylor et al. ("*Taylor*") (U.S. Patent 5,308,621). Applicant respectfully traverses the 35 U.S.C. § 103(a) rejections as such rejections pertain to the cited claims.

The Examiner states that *Schinitsky*, *Murad*, *Herstein*, and *Taylor* were discussed in a prior Office Action (Applicant assumes the Examiner is referring to the Office Action mailed November 19, 2002) and that such discussion has been incorporated into the present Office Action. The Examiner further states that Applicant's arguments have been duly considered, but are deemed unpersuasive. The Examiner also notes that Applicant has argued that none of the prior art suggests having a pH of more than 3.5. However, the Examiner states that *Herstein* (column 10, lines 6-17) teaches that a pH within 3.5 to 4.1 is preferred to facilitate entry of ascorbic acid into the skin and stabilize the ascorbic acid molecule. *See* Office Action, pages 3 and 4.

In order to establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, or in the form of generally available knowledge that one having ordinary skill in the art would have been led to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300, 1301 (Bd. Pat. App. & Int. 1993); *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 U.S.P.Q. 657 (Fed. Cir. 1985). The legal conclusion of obviousness must be supported by facts. See *Graham v. John Deere & Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). Where the legal conclusion is not supported by facts, it cannot stand. *Id.* A rejection based on § 103 clearly must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. The patentability of an invention is not to be viewed with hindsight or "viewed after the event." *Goodyear Company v. Ray-O-Vac Company*, 321 U.S. 275, 279, 64 S.Ct. 593, 88 L.Ed. 721 (1944). The proper inquiry is whether bringing

them together was obvious and not, whether one of ordinary skill, having the invention before him, would find it obvious through hindsight to construct the invention. Accordingly, an Examiner cannot establish obviousness by locating references which describe various aspects of the patent Applicants' invention without also providing objective evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done. An Examiner's unsupported opinion is not objective evidence.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicants' disclosure. *See* MPEP § 2143. *See also In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

As stated above, independent claims 1, 18, and 26 have been amended to require at least about 5.0% (w/v) pre-treated ascorbic acid, having a pH of 3.5 to 4.1, and not having any chemical stabilizers.

Claims 2, 9, and 19 have been cancelled.

Claim 3 has been amended to maintain proper claim dependency.

Schinitsky discloses a composition comprising from about 2 to about 20% ascorbic acid, about 1 to about 10% tyrosine, and about 0.5 to about 5% zinc sulfate. *See Schinitsky*, column 2, lines 38-45. Applicant respectfully suggests that *Schinitsky* does not anticipate, disclose, or suggest Applicant's composition as disclosed in Applicant's amended claims 1, 18, and 26 and the claims depending therefrom, wherein such claims require an aqueous composition of at least 5.0% (w/v) pre-treated ascorbic acid and at a pH of 3.5 to 4.1. Applicant respectfully suggests that *Schinitsky* does not disclose or suggest various features of Applicant's claim(s), particularly a composition having a pH of more than 3.5. Examiner's attempts to remedy the deficiencies of *Schinitsky* by combining with three other references, *Murad*, *Herstein*, and *Taylor*, to arrive at

Applicant's claimed invention, still fall short of an aqueous composition of at least 5.0% (w/v) ascorbic acid and at a pH greater than 3.5.

Murad discloses a composition comprising at least four components: a sugar compound, a primary antioxidant component, at least one amino acid component, and at least one transition metal component. *See Murad*, column 3, lines 25-35. Further, *Murad* prefers an embodiment where the composition is administered orally. In fact, all Examples in *Murad* are directed to compositions in either tablet or capsule form. In a preferred *Murad* embodiment, the composition is administered as a tablet or capsule having about 1 mg to 2,000 mg of *Murad* composition. *See Murad*, column 4, lines 39-50. Further, *Murad* discloses that although any suitable route of administration may be employed, oral administration is preferred. *See Murad*, column 8, lines 43-52. Further, all three routes of administration of the *Murad* composition disclosed in the *Murad* examples comprise orally administrated forms such as capsules (*Murad* Example 1), soft gelatin capsules (*Murad* Example 2), and tablets (*Murad* Example 3). *See Murad*, column 10, lines 5-32. Further, *Murad* claim 1 discloses an orally administered pharmaceutical composition comprising the following *Murad* components: a sugar compound; a primary antioxidant component; at least one amino acid component; and at least one transition metal component. *See Murad*, claim 1. Applicant respectfully suggests that the *Murad* emphasis on oral administration, specifically capsules, soft gelatin capsules, and tablets, teaches away from Applicant's composition having a pH of more than 3.5. Applicant also respectfully suggests that since *Murad* is preferably administered orally, pH is not a critical feature of the *Murad* composition and actually teaches away from Applicant's composition, as discussion of pH, being a measure of the hydronium-ion concentration, is limited to solution-based compositions and is not relevant to the solid-based compositions of *Murad's* tablets and capsules. In fact, pH values have little relevance outside the realm of aqueous-based solutions. Thus, compositions of *Murad* delivered orally in soft gelatin capsules (Example 2) comprising an oil (in which ascorbic acid is only very slightly soluble) are more likely suspensions of ascorbic acid particles, wherein pH again has no relevance.

Herstein discloses a composition comprising two phases. The first *Herstein* phase is a powder phase containing ascorbic acid. The second *Herstein* phase is a liquid emulsion phase containing a stabilizing effective amount of an organoclay composition. *See Herstein*, column 2,

line 65 - column 3, line 6. *Herstein* discloses in great detail the two phases. *Herstein* discloses that the liquid phase comprises an emulsifier that can be selected from various emulsifiers. *See Herstein*, column 4, line 31 - column 6, line 19. *Herstein* maintains that the pH of the combined two-phase composition is preferably maintained within a pH range of 3.5-4.1. *Herstein* further maintains that greater than 82% of the ascorbic acid in his composition remains in the protonated (i.e., ascorbic acid) form. Yet, *Herstein* describes using species such as triethanol amine, sodium hydroxide, and ammonium hydroxide to modulate the pH and maintain it at desired levels. *See Herstein*, column 10, lines 6-23. Applicant contends that the addition of such bases will serve to deprotonate the ascorbic acid, yielding the unstable ascorbate anion. Furthermore, the organoclays described in *Herstein* comprise amine salts that can be expected to complex the ascorbate anion. Thus, while such formulations of *Herstein* are novel in their use of such organoclays to stabilize the ascorbate anion, they cannot be said to comprise 5% ascorbic acid, because such ascorbic acid has been deprotonated. Note that *Herstein* provides no empirical evidence for his above-described claim of 82% protonation.

Taylor discloses the transdermal delivery of micro-sized particles of ascorbic acid. Such micro-sized particles of ascorbic acid are "predominately sized below 20 microns [μm]. More preferably they are predominately in the range of from 2-10 microns." *See Taylor*, column 1, lines 52-55. Such particles are dispersed in a carrier such that "the portion of acetic acid [as particulates] in solution will be less than 0.1% by weight of the composition." *See Taylor*, column 1, lines 59-60. A number of suitable non-aqueous carriers are listed (column 2, lines 20-26) and it is stated that "[p]referably the carrier is essentially water free containing less than about 0.5% by weight water." *See Taylor*, column 2, lines 35-37. The only similarity this reference has with the present Application is the presence of ascrobic acid, albeit in a particulate (solid) form.

Applicant respectfully suggests that there is no motivation or suggestion to combine or modify any of the above-mentioned references. Further, even if there were such motivation or suggestion, one could not arrive at the Applicant's claimed invention comprising an at least about 5%(w/v) aqueous solution of pre-treated ascorbic acid with a pH of 3.5-4.1 and without any chemical stabilizers—as required by independent claims 1, 18, and 26, and associated dependent claims. While some of the above-mentioned references teach compositions

comprising greater than 5% ascorbic acid, such compositions comprise pH values below 3.5 or are in a form in which pH is not relevant (e.g., a tablet); and while some of the above-mentioned references teach compositions with pH values greater than 3.5, such compositions do not comprise greater than 5% ascorbic acid; none of the above-mentioned references, either alone or in combination, teach or suggest a 5% ascorbic acid solution with a pH greater than 3.5. In the absence of treatments described in the present Application, a 5%(w/v) aqueous solution of ascorbic acid will not be stable at pH values greater than 3.5.

As a result of the foregoing, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 3-8, 10-18, and 20-26 under 35 U.S.C. § 103(a) as being unpatentable over *Schinitsky* in view of *Murad*, *Herstein* and *Taylor*.

Accordingly, Applicant respectfully requests that this Application be re-examined in light of Applicant's April 9, 2004 interview with the Examiner, and in light of the above remarks and above-described amendments. Applicant further respectfully requests that the rejections under 35 U.S.C. §§ 102 and 103 be withdrawn and that the claims remaining in the Application be allowed.

Since new claims have not been added, no additional filing fees are believed to be due. Enclosed herewith is a Petition for Two-Month Extension of Time to file the Response, along with a check in the amount of $210.00 for the Petition fee. It is believed that no further fees are due. However, the Director is hereby authorized to charge any fees or credit any overpayment to Deposit Account Number 23-2426 of WINSTEAD SECHREST & MINICK P.C. (referencing number 41758-P001P1C2X1).

If the Examiner has any questions or comments concerning this paper or the present application in general, the Examiner is invited to call the undersigned at (214) 745-5710.

Respectfully submitted,
WINSTEAD SECHREST & MINICK P.C.

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Dated: April 22, 2004

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41758-P001P1C2X1 04/21/2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Meisner, Lorraine

Serial No.: 09/990,611

Filed: 11/21/2001

Title: Ascorbic Acid Composition and Method for Treatment of Aging or Damaged Skin

Art Unit: 1616

Examiner: Choi, Frank I.

Mail Stop: AF
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

AFFIDAVIT OF EDWARD T. MICKELSON

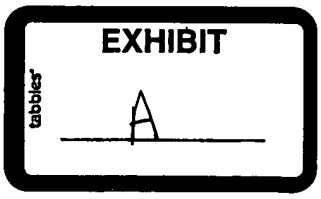
STATE OF TEXAS

COUNTY OF HARRIS

BEFORE ME, the undersigned authority, personally appeared Edward T. Mickelson, who being duly sworn by me, deposed on his oath as follows:

1. "My name is Edward T. Mickelson. I am over 18 years of age, have never been convicted of a felony or a crime of moral turpitude, am of sound mind and fully competent to make this Affidavit.

2. I am a registered patent agent employed by Winstead Sechrest & Minick P.C. and hold a doctorate in chemistry from Rice University (Houston, TX). I have reviewed the statements herein and believe, to the best of my abilities, that they are true and correct.



3. Pursuant to Applicant's April 9, 2004 interview with Examiner Choi and filed concurrently with Applicant's response to the Office Action mailed December 18, 2003, Applicant hereby provides the requested affidavit (as Exhibit A) detailing the levels of ascorbic acid in the compositions of Duffy et al. ("*Duffy*") (U.S. Patent 5,516,793).

4. Claims 1-3, 10, 15-18, 24, and 25 of the above-identified Application have been rejected under 35 U.S.C. § 102(b) as being unpatentable over Duffy et al. ("*Duffy*") (U.S. Patent 5,516,793).

5. The Examiner has stated that *Duffy* expressly discloses a composition comprising demineralized water, propylene glycol, glycerin, hydroxyethylcellulose, Tween 20, ammonium hydroxide, glycolic acid and ascorbic acid (5% or 10%), having a pH of 3.7 (5%) and 3.8 (10%). The Examiner has also stated that with respect to claim 24, the term "about 15%" is not defined, as such, the Examiner has read the term "about" to include 10%. *See* Office Action, page 2, fourth full paragraph.

6. All of the above-rejected claims require a composition comprising at least 5.0% (w/v) ascorbic acid in water, and a pH greater than 3.5. Such compositions, comprising relatively high pH values for such relatively high concentrations of ascorbic acid, are made possible by the stabilizing treatments described in Application. Without such treatments, the ascorbic acid rapidly degrades at pH values greater than 3.5 to yield solutions that comprise less than 5.0%(w/v) ascorbic acid. With regard to *Duffy*, Applicant respectfully points out that the Examiner is assuming that there is no reaction of components within the mixtures and that the resulting compositions of *Duffy* are simply the sum of the initial components. Reaction of the components of *Duffy* does occur, however, and the resulting compositions disclosed therein do not comprise at least 5.0% (w/v) ascorbic acid in the admixed formulation.

7. *Duffy* describes the addition of ascorbic acid to topical formulations for the purpose of reducing irritation caused by another active ingredient. Unlike in the compositions of the present invention, however, ascorbic acid is not the active ingredient in the compositions of *Duffy*. Referring to *Duffy*, col. 7, ll. 8-31 (Example II), Compositions E and F are formulated (in part) with 5 and 10wt.% ascorbic acid, and have resulting pH values of 3.7 and 3.8, respectfully. However, in each of these compositions, sufficient base (ammonium hydroxide) is added to convert all or most of the ascorbic acid present in the formulation to the unstable ascorbate anion (with is easily oxidized).

8. Composition E comprises the following:

2.700 wt% ammonium hydroxide (NH_4OH), M.W. = 35 g/mol

4.000 wt% glycolic acid ($CH_2OHCOOH$), M.W. = 76 g/mol

5.000 wt% ascorbic acid ($C_6H_8O_6$), M.W. = 176 g/mol

9. Assuming 100 grams total (total amount is really arbitrary, but this assumption simplifies the calculation. Note that *Duffy* never actually listed amounts).

10. Molar amounts are calculated as follows:

Ammonium hydroxide = 2.700 g ÷ 35 g/mol = 0.077 mol, normalized to 2.8

Glycolic acid = 4.000 g ÷ 76 g/mol = 0.053 mol, normalized to 1.9

Ascorbic acid = 5.000 g ÷ 176 g/mol = 0.028 mol, normalized to 1

11. Thus, there is roughly three times as much NH_4OH (on a mole basis) as ascorbic acid in *Duffy's* Composition E. Even if it is assumed that the NH_4OH preferentially "neutralizes" all of the glycolic acid present, there is still enough NH_4OH present to convert more than 85% of the ascorbic acid to the ascorbate anion, as shown in the calculation below:

0.077 mol ammonium hydroxide – 0.053 mol glycolic acid = 0.024 mol ammonium hydroxide.

0.028 mol ascorbic acid – 0.024 mol ammonium hydroxide = 0.004 mol ascorbic acid remaining.

0.004 mol ascorbic acid x 176 g/mol = 0.70 g ascorbic acid remaining, or about 0.7 wt% in the composition.

12. Composition F comprises the following:

4.300 wt% ammonium hydroxide (NH_4OH), M.W. = 35 g/mol

4.000 wt% glycolic acid ($CH_2OHCOOH$), M.W. = 76 g/mol

10.000 wt% ascorbic acid ($C_6H_8O_6$), M.W. = 176 g/mol

13. Assuming 100 grams total:

Molar amounts are calculated as follows:

Ammonium hydroxide = 4.300 g ÷ 35 g/mol = 0.12 mol, normalized to 2.3

Glycolic acid = 4.000 g ÷ 76 g/mol = 0.053 mol, normalized to 1

Ascorbic acid = 10.000 g ÷ 176 g/mol = 0.057 mol, normalized to 1.1

14. Thus, there is enough NH_4OH present to convert all of both the glycolic acid and ascorbic acid to their conjugate base forms (the ascorbate anion in the case of ascorbic acid). Thus, such compositions of *Duffy* cannot be expected to comprise any more than about 1wt.% ascorbic acid in their final admixed form.

FURTHER AFFIANT SAYETH NOT

Edward T. Mickelson

SUBSCRIBED and SWORN TO BEFORE ME, the undersigned authority, on this the 19th day April, 2004.

JUDY K. JACKSON
Notary Public
State of Texas
My Comm. Expires 10-2-2007

NOTARY PUBLIC IN AND FOR THE STATE OF TEXAS